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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,970	07/19/2002	Tai-Tung Yip	16866-38-1PC	6649

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,970	YIP ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,12,20 and 84-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,12,20 and 84-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Yip et al.

Response to the Amendment

The Amendment filed on 1/18/2006 in response to the previous Final Office Action (12/21/2005) is acknowledged and has been entered. The Final Office action mailed on 12/12/2005 has been withdrawn upon reconsideration.

Claims 1, 8, 12, 20 and 84-94 are currently pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

New Rejections necessitated by reconsideration:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8, 12, 20, 84-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims read on a method of diagnosing prostate cancer versus benign prostate hyperplasia comprising: (1) obtaining from a subject a sample containing a plurality of prostate related protein markers having an apparent molecular weight below 10,000 Da; (2) determining by mass spectroscopy a test amount of the plurality of protein markers in the sample, the protein markers having an apparent molecular weight of less than 10,000 Da; (3) comparing the test amount of the plurality of markers having apparent molecule weight of less than 10,000 Da with an amount of a plurality of protein markers having an apparent molecular weight of less than 10,000 Da from a control sample where the control sample originates from benign prostate hyperplasia; and (4) determining whether the test amount is a diagnostic amount consistent with the diagnosis of prostate cancer versus benign prostate hyperplasia. Thus, the claims read on using proteomic patterns as a diagnosis of prostate cancer versus benign prostate hyperplasia.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to using proteomic patterns as a diagnosis of prostate cancer versus benign prostate hyperplasia. The specification teaches (beginning on page 30, Examples) that protein markers were identified using a Ni(II) ProteinChip® Array, H4 ProteinChip® array, and a SCX1 ProteinChip® array, wherein the samples, specifically seminal plasma, were obtained from one BPH (benign prostate hyperplasia) patient and one patient with prostate cancer. With regards to the Ni(II) ProteinChip ® array, the specification teaches (page 30, line 28 to page 32, line 12 and Figure 4) that a number of proteins such as proteins having an apparent molecular weight of about 2776 Da, 4423 Da, 4480 Da, 5753 Da, 6098 Da, 6270 Da, 6998 Da, 8030 Da and 8714 Da, were found to be very abundant in the

sample from the prostate cancer patient than in the sample from the BPH patient. Moreover, the specification teaches (page 30, line 28 to page 32, line 12 and Figure 4) that a number of proteins such as proteins having an apparent molecular weight of about 2776 Da, 2905 Da, 3038 Da, 3600 Da, 3835 Da, 3933 Da and 4175 Da, were found to be very abundant in the sample from the BPH patient than a sample from the prostate cancer patient. With regards to the H4 ProteinChip ® array, the specification teaches (page 32, line 15 to page 33, line 23, and Figure 5) that a number of proteins such as proteins having an apparent molecular weight of about 2776 Da, 5753 Da, 6098 Da, 6270 Da, 6998 Da, 7843 Da, 8030 Da and 8240 Da were found to be very abundant in the sample from the prostate cancer patient than the samples from the BPH patient. Furthermore, the specification teaches (page 32, line 15 to page 33, line 23, and Figure 5) that a number of proteins such as proteins having an apparent molecular weight of about 2776 Da, 6098 Da, 6270 Da, 6998 Da, 7843 Da and 8030 Da were also bound and detected using the Ni (II) ProteinChip ® array. With regards to SCX1 ProteinChip® array, the specification teaches (page 33, line 25 to page 34, line 23 and Figure 6) that a protein having an apparent molecular weight of about 5753 Da was present at a high level (relative intensity of about 52) in the sample of the prostate cancer patient. Thus, while the specification appears to suggest proteomic patterns which may be used to discriminate between benign prostate hyperplasia and prostate cancer for the two individuals samples, the specification appears to be silent on whether the proteomic profiles obtained from these two individuals is indicative of all patients suffering from either benign prostate hyperplasia and prostate cancer.

In the instant case, those of skill in the art recognize the unpredictability of using proteomic profiling in a diagnostic setting. For example, Diamandis, E.P. (J. National Cancer Institute 2004; 96: 353-356) discusses the potential problems in the analysis of serum proteomic patterns for early cancer diagnosis. These problems for identifying tumor markers include the mechanisms by which tumor markers are released into the circulation, their abundance in biologic fluids, their metabolism and excretion, their dynamic relationship within the host, the clinical samples used, the mass spectrometry instrument and/or the bioinformatic analysis (page 353, 1st column, 3rd paragraph). For instance, Diamandis teaches that discrepancies in the discriminatory peaks (i.e., peaks representing molecules that appear or disappear during cancer progression, or whose amounts differ in cancerous versus noncancerous tissue) identified by four different papers by three different

research groups suggests that serum proteomic patterns obtained by the SELDI-TOF technique may not be reproducible within a group or among groups of investigators for the same type of cancer, even when the general analytical methods or datasets are the same (page 353, 1st column, 4th paragraph). Regarding the clinical samples, Diamandis teaches that it is still unknown whether the proteomic patterns will differ between plasma and serum, or how they are affected by the number of freeze thaw cycles or its length of storage (page 354, 1st column, last paragraph). More recently, Diamandis et al. (Clinical Cancer Research 2005; 11: 963-965) teach that while the original papers on serum proteomic profiling for diagnosis of various forms of cancer reported impressive results, these results have not been reproduced by other laboratories and the method has not been validated (page 964, 2nd column, 1st full paragraph). Specifically, Diamandis et al. teach that using peaks of unknown identity for diagnostic purposes should not be a reason a reason to invalidate the method; instead, as Ranshoff points out, it will be important to examine "if this technology does work" and leave the question of "how it works" for investigation at a later time. However, Diamandis points out that precautionary measures about sample collection, processing, and patient selection must be seriously considered to avoid biases (page 964, 2nd column, 1st full paragraph). Along the same lines, Grizzle et al. (Cancer Informatics 2005; 1: 86-97) teach that the use of any multiplex mass spectroscopy based approach, as in the analysis of bodily fluids to detect a disease, must be analyzed with great care due to the susceptibility of multiplex and mass spectroscopy methods to biases introduced via experimental design, patient samples, and/or methodology (abstract) In particular, Grizzle et al. teach that specific biases include those related to experimental design, patients, samples, protein chips, chip reader and spectral analysis (abstract). Regarding the biases based on patients, Grizzle et al. teach that these biases include demographics (e.g., age, race, ethnicity, sex), homeostasis (e.g., fasting, medications, stress, time of sampling), and the site of analysis (hospital, clinic other) (beginning on page 88, 2nd column to page 92, 1st column). Regarding the biases in samples, Grizzle et al. teach that the biases in samples include conditions of sampling (type of sample container, time of processing, time to storage), conditions of storage (time and temperature of storage), and prior manipulation (freeze thaw cycles)(beginning on page 92, 1st column to page 93, 1st column). experimental design, patient samples, and/or methodology (abstract). These references demonstrate that there are a number of different biases that need to be considered prior to providing a diagnosis of a diseases based on proteomic profiling.

Thus, in order to practice the claimed invention, the skilled artisan would have had to engage in a large amount of experimentation to practice the claimed invention. In view of the lack of guidance and the large amount of experimentation in an unpredictable art, it would require undue experimentation to practice the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8, 12, 20 and 84-94 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 1-14 of copending Application No. 10/221,905.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. For example, the specific protein markers having a molecular weight of 97402.68, 9752.30, 8766.93, 6277.97, or 2781.72 Da claimed in the conflicting application anticipates the genus of a markers having an apparent molecular weight of less than 10,000 Da claimed in the application being examined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 8, 12, 20 and 84-94 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 1-8 of copending Application No. 10/505,367.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. For example, the specific protein markers having a molecular weight of 3448, 4036, ... 8445 Da claimed in the conflicting application anticipates the genus of a markers having an apparent molecular weight of less than 10,000 Da claimed in the application being examined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 8, 12, 20 and 84-94 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 1-8 of copending Application No. 10/513,649.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus. For example, the specific protein markers having a molecular weight of 4475, 5074, 5382, ... 9656 Da claimed in the conflicting application anticipates the genus of a markers having an apparent molecular weight of less than 10,000 Da claimed in the application being examined.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Therefore, NO claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

SUPERVISORY PATENT EXAMINER
2/17/06